

POT MARIGOLD (*Calendula officinalis* L.) – A POSITION IN CLASSICAL PHYTOTHERAPY AND NEWLY DOCUMENTED ACTIVITIES

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ABSTRACT

The flower (inflorescence, basket-type inflorescence) of marigold (*Calendulae officinalis flos*) is a well-known plant raw material in traditional phytomedicine. It has a complex chemical composition, dominated by flavonoids and terpenoids. Terpenoids are mainly represented by oleanolic acid derivatives specific for this species: triterpenoid saponins – calendulosides A–H and triterpenoid glycosides, so-called calendulaglycosides A and B. Biological activity profiles of the raw material, such as anti-inflammatory, antimicrobial, immunostimulatory and antioxidant properties, determine its use especially in the treatment of dermatological diseases. In addition to spasmolytic, hypolipemic and antidiabetic properties of this flower, scientific studies also demonstrated its cardioprotective, hepatoregenerative, pancreas-regenerating, neuroprotective and even anticancer health-promoting effects. Moreover, *C. officinalis* is used in the cosmetology and food industry.

Key words: marigold, medicinal plant, chemical composition, therapeutic properties, cosmetic application

GENERAL CHARACTERISTICS OF THE SPECIES AND POSITION IN MEDICINE

Calendula officinalis L. is a species belonging to the family *Asteraceae*, formerly *Compositae*. The name of the species – *Calendula* – comes from the Latin word *calends*, meaning the first day of each month, which is associated with the flowering periods of the plant [Basch et al. 2006, Arora et al. 2013, John et al. 2017]. *C. officinalis* is an annual or biennial herbaceous plant, reaching from 30 to 60 cm in height. Distinctive features of the plant's appearance are heterophylly (in a single individual, the lower leaves are ovoid and upper are lanceolate) and the basket-type inflorescence composed of two types of flowers (so-called ligular flowers on the external side of the inflorescence, and tubular flowers on the internal side).

Typically, the inflorescences are yellow-orange, but there are also marigold cultivars with light-yellow and dark-orange flowers. The flowering period of marigold in Europe is from June to September. Importantly, all parts of the plant are covered with glandular hairs of a multicellular structure where the essential oil is produced [Arora et al. 2013, European Pharmacopoeia 9.0 2017, Farmakopea Polska XI 2017].

Natural marigolds localities are found in Europe in the Mediterranean region and the Middle East. Currently, it is a widespread and valued plant cultivated for medicinal and ornamental purposes also in other parts of Europe (the Balkans, Eastern Europe and Germany) as well as in North America [Basch et al. 2006, John et al. 2017].

Marigold inflorescence is a long-known healing raw material in folk medicine. The first written records

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about its application date back to the 12th century [Bingen 1155]. Traditionally, it has been used externally to treat small wounds, burns and other skin problems. This application in dermatological diseases, also known today, has been the subject of previous reviews regarding *C. officinalis* [Arora et al. 2013, Leach 2008, Muley et al. 2009, Paul et al. 2018, Preethi and Kuttan 2009, Shafeie et al. 2015].

Mature, dried marigold flowers (syn. calendula inflorescences, calendula baskets, calendula basket inflorescence) – *Calendulae flos* – are currently used as pharmaceutical raw material in official phytotherapy. A monograph with such a title is listed in the European Pharmacopoeia 9th [European Pharmacopoeia 9.0 2017]. According to pharmacopoeial guidelines, the raw material should contain more than 0.4% of flavonoids, calculated per hyperoside [European Pharmacopoeia 9.0 2017].

Calendula flower also has a positive opinion of the European Scientific Cooperative on Phytotherapy [ESCOP] and the Committee on Herbal Medicinal Products (HMPC) specifically appointed by the European Medicines Agency [EMA]. Since 2004, this raw material has been also described in a monograph entitled *Flos Calendulae* in the International Pharmacopoeia issued by the World Health Organization [WHO 2002]. The raw material has been also much longer included, since 1986, in phytotherapeutic monographs issued by German Commission E Monographs, Phytotherapy [1986].

In addition, *C. officinalis* is accepted by the European Commission as a safe cosmetic ingredient [CosIng].

BIOACTIVE COMPONENTS

Many secondary metabolites are responsible for the biological activity of *C. officinalis*. The main group are flavonoid compounds, among others, aglycones: quercetin, isoquercetin, rutin, and glycosides: quercetin-3-rutinoside, isorhamnetin-3-neohesperidoside (calendoflavoside) and quercetin 3-neohesperidoside (calendoflavobioside) (Fig. 1, Tab. 1) [Arora et al. 2013, Khalid and Silva 2012]. Calendoflavoside is another specific compound belonging to the flavonoids that has been isolated for the first time from the marigold's inflorescence in 1989 (Fig. 1, Tab. 1) [Miguel et al. 2016].

Terpenoids are an important group of secondary metabolites, which occur in the *C. officinalis* inflorescence and are responsible for its biological activity [Arora et al. 2013, Muley et al. 2009]. It is possible to distinguish in this group of compounds triterpenoid monoesters: esters of faradiol (faradiol-3-O-palmitate, faradiol-3-O-myristate, faradiol-3-O-laurate), esters of arnidiol (arnidiol-3-O-palmitate, arnidiol-3-O-myristate, arnidiol-3-O-laurate) and specific for *C. officinalis* – calenduladiol and its esters (calenduladiol-3-O-palmitate, calenduladiol-3-O-myristate) [Arora et al. 2013, Khalid and Silva 2012]. Derivatives of oleanolic acid – triterpenoid saponins: calendulosides A–H are an important, specific for *C. officinalis* compounds from the group of terpenoids (Fig. 2, Tab. 1) [Arora et al. 2013, Khalid and Silva 2012, Muley et al. 2009]. Triterpenoid glycoside derivatives of oleanolic acid, so-called calendulaglycoside A and B and their esters are also characteristic compounds that occur only in this species (Fig. 3, Tab. 1) [Grzelak and Janiszowska 2002, Ukiya et al. 2006, Wiktorowska et al. 2010, Farahpour 2014].

The presence of coumarins (esculetin, scopoletin, umbelliferone), lipids (phospholipids, glycolipids), fiterosterols, aminoacids (alanine, leucine, lysine, methionine) and saccharides has been also documented in *C. officinalis* inflorescences (Tab. 1) [Arora et al. 2013, Khalid and Silva 2012].

In addition, compounds from the carotenoid group: α - and β -carotene, flavoxanthin, luteoxanthin, lycopene and lutein and its derivatives were mainly isolated in the extracts of marigold flowers as well as in pollen and leaf extracts (Tab. 1) [Muley et al. 2009, Arora et al. 2013, Khalid and Silva 2012, Legha et al. 2012].

An important raw material obtained from *C. officinalis* flowers is an essential oil containing mainly terpenoid compounds from the monoterpene group, such as limonene, α -pinene, β -pinene, α -thujene, sabinene, *p*-cymene and sesquiterpenoids, e.g. α -humulene, α -yangelene, germacrene D and nerolidol (Tab. 2). The percentage of essential oil content in inflorescences depends on the stage of plant development. The largest production takes place during the flowering period of the plant [Muley et al. 2009, Khalid and Silva 2012, Arora et al. 2013].

Characteristic metabolites of the family *Asteraceae* species are polysaccharides that affect the immune

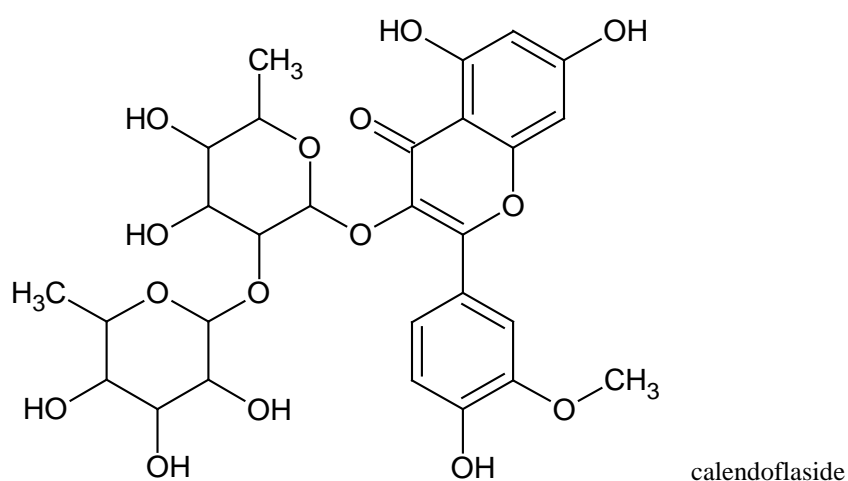
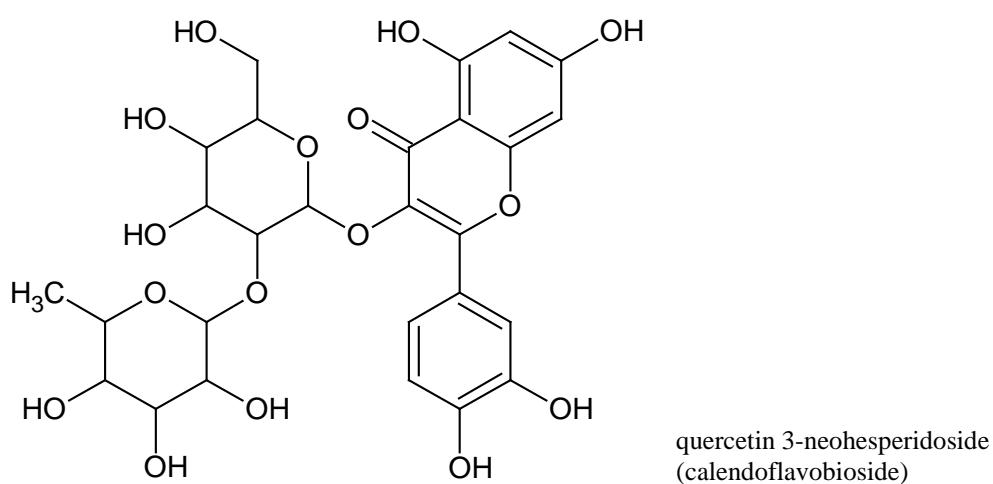
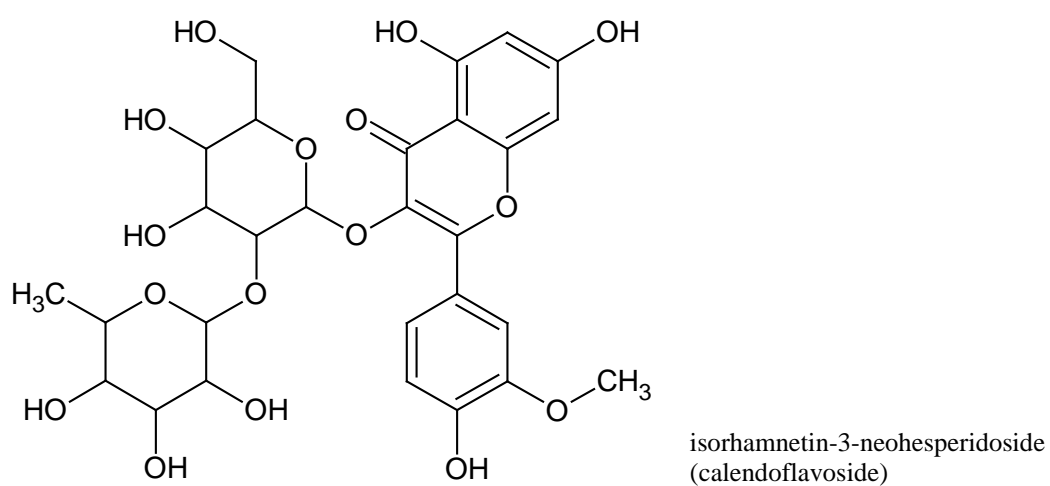
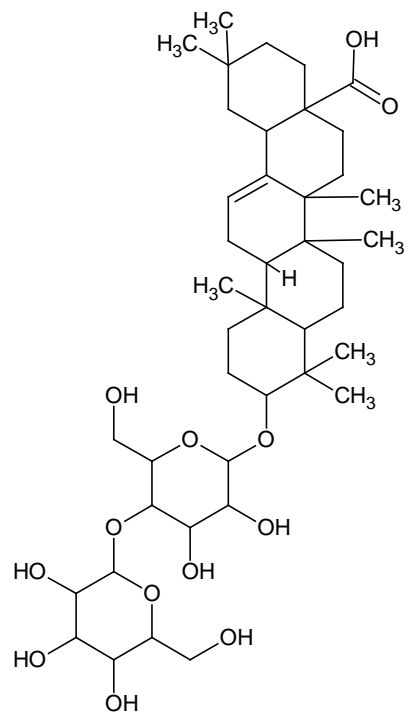
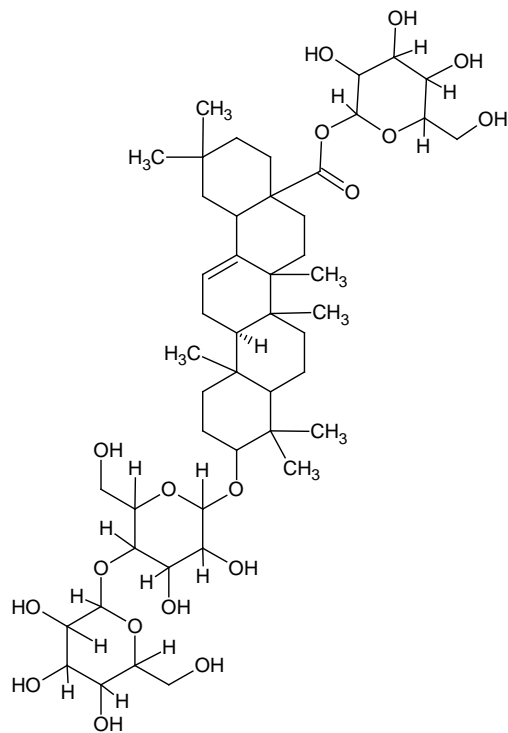


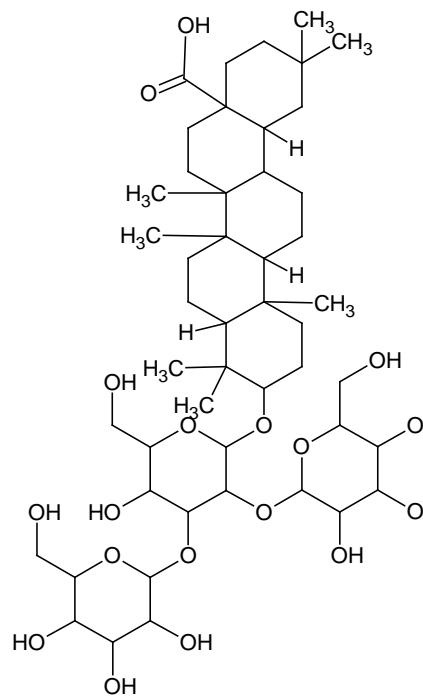
Fig. 1. Chemical structures of flavonoids specific for *C. officinalis*



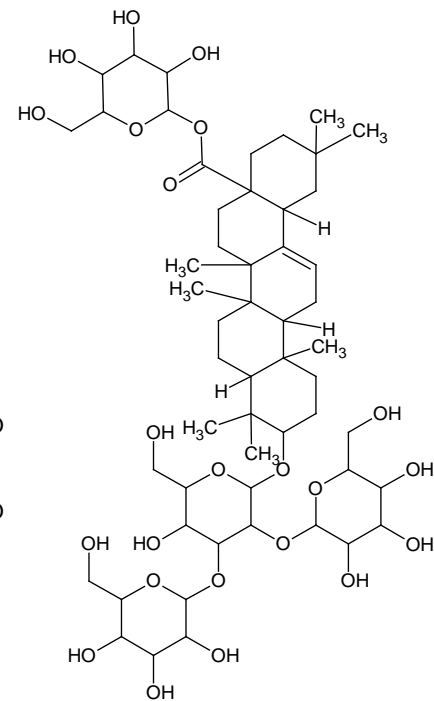
calenduloside A



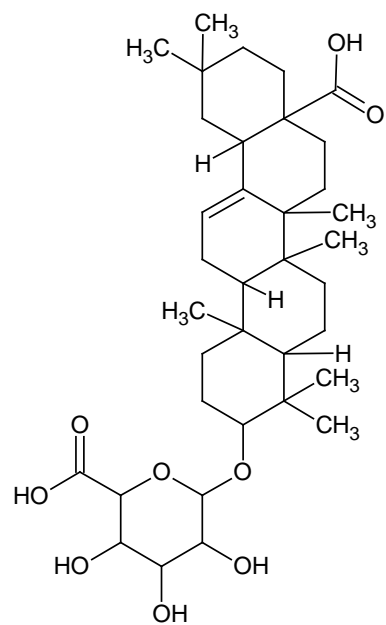
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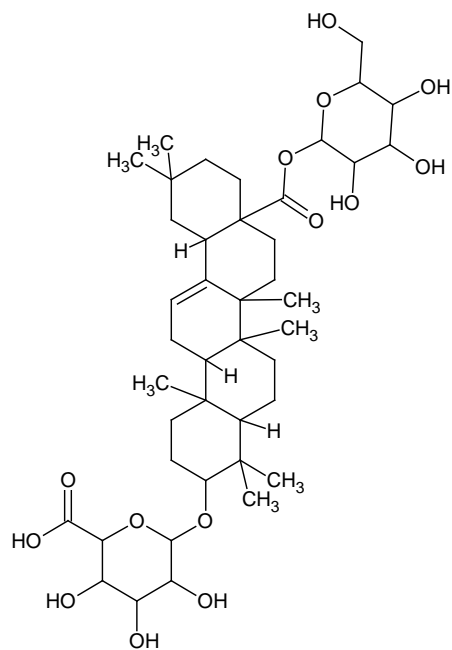
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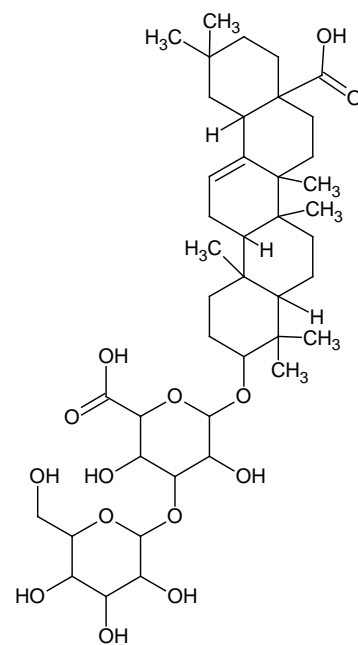
calenduloside D



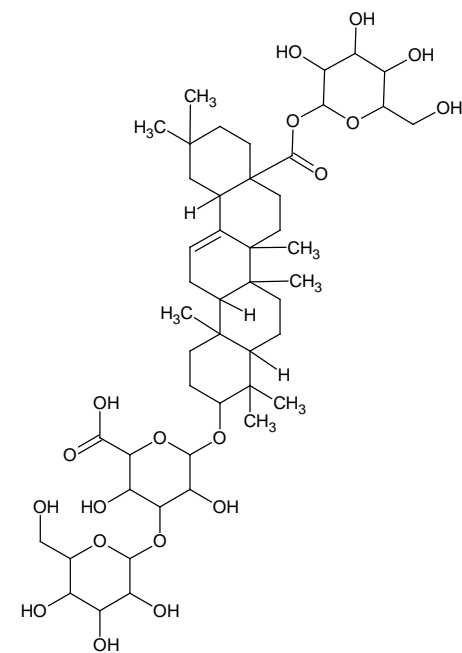
calenduloside E



calenduloside F



calenduloside G



calenduloside H

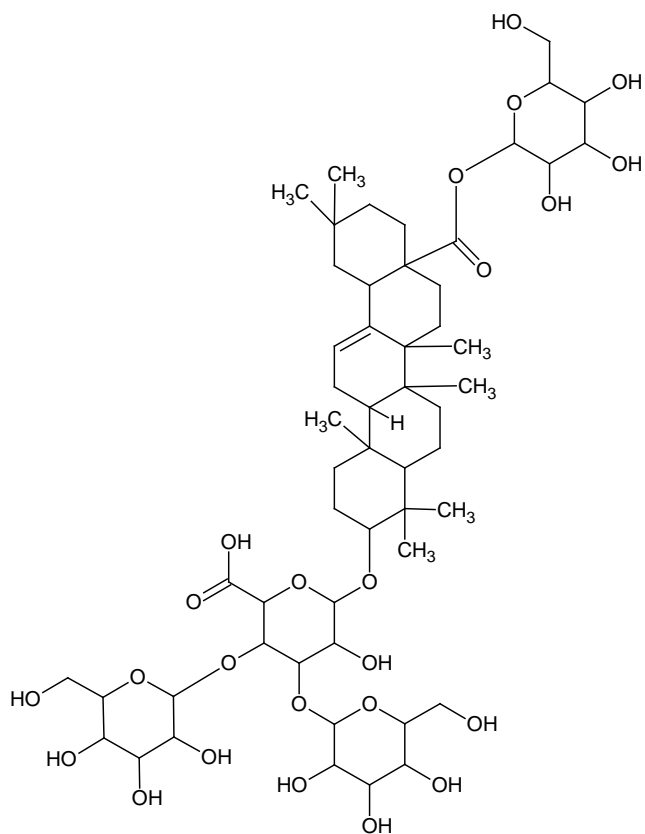
Fig. 2. Chemical structures of *C. officinalis*-specific triterpenoid saponins (oleanolic acid derivatives): calendulosides A–H

Table 1. Chemical composition of *C. officinalis*

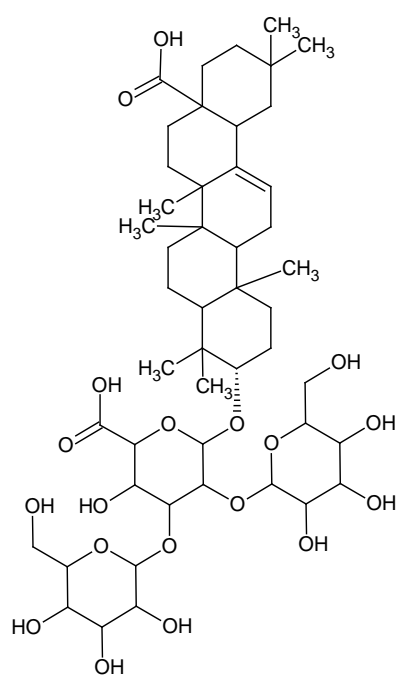
| Group of secondary metabolites | | Compounds | References |
|--------------------------------|--------------------------|--|---|
| Flavonoids | aglycones | isoquercitrin, narcissin, quercetin, rutinoid | Ukiya et al. 2006, Kurkin and Sharova 2007, Hernández-Saavedra et al. 2016, Miguel et al. 2016 |
| | glycosides | calendoflaside, isorhamnetin-3-neohesperidoside (calendoflavoside), quercetin 3-neohesperidoside (calendoflavobioside), quercetin-3-O-rutinoid | |
| Terpenoids | triterpenoids | erythrodiol, monoesters of lupeol, taraxasterol, ursadiol | Neukirch et al. 2004, Ruszkowski et al. 2005, Ukiya et al. 2006, Muley et al. 2009, Arora et al. 2013, Nizyński et al. 2015, Miguel et al. 2016, John et al. 2017 |
| | triterpendiol monoesters | calenduladiol and its esters (calenduladiol-3-O-palmitate, calenduladiol-3-O-myristate), esters of arnidol (arnidiol-3-O-palmitate, arnidol-3-O-myristate, arnidol-3-O-laurate), esters of faradiol (faradiol-3-O-palmitate, faradiol-3-O-myristate, faradiol-3-O-laurate) | |
| | triterpenoid saponins | calendulosides A–H | |
| | triterpenoid glycosides | calendulaglycosides A and B and their esters: calendulaglycoside A 6-O-n-methyl ester, calendulaglycoside A 6-O-n-butyl ester, calendulaglycoside B 6-O-n-butyl ester, glucuronides A, B, C, D, F | |
| Carotenoids | | auroxanthin, α -cryptoxanthin, α -carotene, β -carotene, β -cryptoxanthin, flavoxanthin, lutein and its derivatives (9/9A-lutein, 13/13 Z-lutein), luteoxanthin, lycopene, neoxanthin, 9Z-neoxanthin, violaxanthin, 9Z-violaxanthin | Muley et al. 2009, Legha et al. 2012, Arora et al. 2013, John et al. 2017 |
| Coumarins | | esculetin, scopoletin, umbelliferone | Bakó et al. 2002 |
| Lipids | | fatty acids: lauric acid, palmitic acid, stearic acid, linoleic acid, glycolipids, phospholipids | John et al. 2017 |
| Fitosterols | | stigmasterol, sitosterol | Muley et al. 2009, Arora et al. 2013 |
| Amino acids | | alanine, arginine, aspartic acid, histidine, glutamic acid, leucine, lysine, methionine, phenylalanine, proline, serine, tyrosine, valine | Muley et al. 2009, Arora et al. 2013, John et al. 2017 |
| Saccharides | | arabinogalactan, neohesperidose and its derivatives, ramnoarabinogalactan | Muley et al. 2009, Arora et al. 2013 |
| Benzofurans | | calendin | Colombo et al. 2015, John et al. 2017 |

Table 2. Chemical composition of *C. officinalis* essential oil [Okoh et al. 2007, John et al. 2017]

| Terpenoid compounds of <i>C. officinalis</i> essential oil | |
|--|--|
| Monoterpenoids | 1,8-cineol, p-cymene, geraniol, limonene, ocimene, trans- β -ocimene, α -pinene, β -pinene, sabinene, α -terpineol, terpinen-4-ol, α -thujene |
| Sesquiterpenoids | calarene, cadina-1,4-diene, δ -cadinen, α -cubebene, germacrene D, α -humulene, α -kadinol, nerolidol, T-murolol, epi-bicyclo-sesquiphellandrene, α -ylangene |



calendulaglycoside A



calendulaglycoside B

Fig. 3. Chemical structures of *C. officinalis*-specific triterpenoid glycosides (glycosides of oleanolic acid): calendulaglycoside A and B

Table 3. Biological activity and mechanisms of *C. officinalis* effects confirmed by scientific research

| Biological activity | Mechanism of action | References |
|-------------------------------------|---|---|
| Anti-inflammatory activity | inhibition of ear edema in mice induced by irritants (flower extract containing faradiol monoesters), reduction of burn swellings in rats by using a cream with the addition of ethanol flower extract, inhibition of proinflammatory cytokines (IL-1 β , IL-6, TNF- α and IFN- γ) and C-reactive protein (CRP) in mice with induced inflammation by lipopolysaccharide (LPS) injection (ethanol flower extracts), reduced inflammatory bone resorption (oral administration of the flower extract), reduction of symptoms of bacterial vaginosis in women of childbearing age (cream with flower extracts), reduction of myeloperoxidase, lactate dehydrogenase and lipid peroxidase activity in rat colitis (methanol flower extracts) | Alexandre et al. 2018, Arora et al. 2013, Banakar et al. 2016, Farahpour 2014, Muley et al. 2009, Parente et al. 2012, Singh et al. 2011, Ukiya et al. 2006 |
| Wound healing acceleration activity | increased granulation tissue formation by accelerating the metabolism of collagen, nucleoproteins and glycoproteins (flower extracts), increase in the rate of new blood vessel formation in skin wounds in rats (water flower extracts), reduction of collagenase activity (water and methanol extract from flowers and leaves), an increase in the rate of wound healing in patients with venous leg ulceration (hydroglycolic flower extracts), acceleration of healing, reduction of infection, itching, redness, pain in foot injuries in people with diabetes (cream with flower extracts), increase in the proliferation and migration of fibroblasts in human lung fibroblast cells, Swiss albino mouse fibroblast cells and human primary dermal fibroblast cells (ethanol flower extracts) | Buzzi et al. 2016, Dinda et al. 2015, Gilca et al. 2018, Lovecka et al. 2018, Nicolaus et al. 2017, Paul et al. 2018 |
| Antibacterial activity | Gram (+) bacteria: <i>Actinomyces odontolyticus</i> , <i>Bacillus subtilis</i> , <i>Enterococcus faecalis</i> , <i>Micrococcus luteus</i> , <i>Peptostreptococcus micros</i> , <i>Staphylococcus aureus</i> , <i>Streptococcus mutans</i> (water and methanol flower extracts), Gram (–) bacteria: <i>Agrobacterium tumefaciens</i> , <i>Burkholderia glathei</i> , <i>Caphocytophaga gingivalis</i> , <i>Eikenella corrodens</i> , <i>Escherichia coli</i> , <i>Furobacterium nucleatum</i> , <i>Porphyromonas gingivalis</i> , <i>P. intermedia</i> , <i>Prevotella</i> spp., <i>Pseudomonas aeruginosa</i> , <i>P. syringae</i> , <i>Veilonella parvula</i> , <i>Vibrio cholerae</i> (water and methanol flower extracts) | Arora et al. 2013, Khalid and Silva 2012, Lovecka et al. 2018, Muley et al. 2009, Shankar et al. 2017, Singh et al. 2011 |
| Antifungal activity | growth inhibition of <i>Candida</i> strains: <i>C. albicans</i> , <i>C. dubliniensis</i> , <i>C. glabrata</i> , <i>C. krusei</i> and <i>C. parapsilosis</i> (flower essential oil), growth inhibition of strains: <i>Geotrichum candidum</i> , <i>Microsporum canis</i> , <i>M. gypseum</i> , <i>T. mentagrophytes</i> , <i>Trichophyton rubrum</i> (methanol flower extracts) | Faustino et al. 2018, Khalid and Silva 2012, Lovecka et al. 2018, Saffari et al. 2017 |
| Antiviral activity | inhibition of HIV replication (organic solvent flower extracts), inhibition of herpes and influenza virus (flower tincture), moderate inhibitory effect on Epstein-Barr virus (EBV-EA) (<i>C. officinalis</i> triterpenoid glycosides) | Muley et al. 2009, Salehi et al. 2018, Ukiya et al. 2006 |
| Antitrichomona activity | growth inhibition of <i>Trichomonas vaginalis</i> protozoan (components of the essential oil) | Samochowiec et al. 1979 |

Table 3 cont.

| Biological activity | Mechanism of action | References |
|--|--|---|
| Antioxidant activity | reduction of superoxide and hydroxyl radicals (butanol flower extracts), increase in the concentration of reduced glutathione (GSH), superoxide dismutase (SOD) and catalase (CAT) in periodontitis in rats (aqueous flower extracts), reduction of production of reactive oxygen species (ROS) in skin cells treated with H ₂ O ₂ (ethanol flower extracts), inhibition of lipid peroxidation in rat liver microsomes (butanol flower extracts), reduction of malondialdehyde (MDA) concentration in periodontitis in rats (water flower extracts) | Cordova et al. 2002, Farahpour 2014, Lima et al. 2017, Xuan et al. 2016 |
| Skin brightening effect | inhibition of melanin production induced by alpha melanocyte-stimulating hormone in melanoma cells (flower ethyl acetate extracts) | Xuan et al. 2019 |
| Spasmolytic activity | inhibition of spontaneous intestine contractions (water-ethanol flower extracts) | Arora et al. 2013, Muley et al. 2009 |
| Antidiabetic and hypolipemic activity | reduction in blood and urine glucose levels in diabetes-induced rats (water-ethanol flower extract), restoration of normal blood and urine glucose concentration and blood lipids in diabetes-induced rats (high doses of water-ethanol flower extracts), reduction in blood glucose levels in hyperglycemic rabbits (extracts from <i>C. officinalis</i> , <i>Salvia officinalis</i> , <i>Glycyrrhiza glabra</i> , <i>Echinacea purpurea</i>), increase in liver glycogen levels in hyperglycemic rabbits (extracts from <i>C. officinalis</i> , <i>Salvia officinalis</i> , <i>Glycyrrhiza glabra</i> , <i>Echinacea purpurea</i>) | Singh et al. 2011, Aghajanyan and Trchounian 2018, Singh et al. 2011 |
| Hepatoprotective and hepatoregenerative activity | reduction of hepatocytolysis and inhibition of aspartate aminotransferase, alanine aminotransferase, lactate dehydrogenase, succinate dehydrogenase and cyclooxygenases activities (water-ethanol flower extracts), increase in the activity of reduced glutathione enzymes, superoxide dismutase, catalase and increase of adenosine triphosphate content in hepatocytes in the rat model of acute hepatitis (flower extracts) | Muley et al. 2009, Singh et al. 2011, Toropova et al. 2017 |
| Pancreas regenerating activity | increase in the production of nucleic acids, proteins, pancreatic amylase, and eduction of pancreatic oxidative stress in cells of the pancreatic parenchyma (ethanol flower extracts) | Kaur et al. 2016 |
| Cardioprotective activity | cardioprotective effect by regulating blood pressure and flow in the aorta and left ventricle (flower extracts), reduction in the extent of myocardial infarction and cardiomyocyte apoptosis in induced ischemic disease in rats (flower extracts) | Singh et al. 2011 |
| Neuroprotective activity | reduction of oxidative damage and striatal neuronal loss in rats with induced neurotoxicity (ethanol flower extracts) | Shivasharan et al. 2013 |
| Antitumor activity | cytotoxic effect on cell lines: colon cancer, leukemia, melanoma and breast cancer (<i>C. officinalis</i> triterpenoid glycosides), cytotoxic effect on Ehrlich tumor (flower extracts), inhibiting the growth of human liver cancer cells (flower extracts), inhibition of cell proliferation in human embryonic kidney (HEK 293T) and human liver cancer (HepG2) cell lines (ethanol and aqueous flower extracts) | Lovecka et al. 2018, Muley et al. 2009, Ukiya et al. 2006 |
| Immunostimulatory activity | increase in cell phagocytosis (<i>C. officinalis</i> polysaccharide fraction) | Arora et al. 2013, Muley et al. 2009 |

system and sesquiterpenoid lactones with various biological activities. Marigold flowers were shown to contain polysaccharides (among others neohesperidoside and its derivatives, arabinogalactan, rhamnoarabinogalactan) with immunostimulatory properties, and sesquiterpenoid lactone – calendin (bitter constituent) [Muley et al. 2009, Arora et al. 2013, Colombo et al. 2015].

Interestingly, the sugar part of glycosidic combinations present in flowers may be formed by lactose (milk sugar), which is a huge rarity in the plant kingdom. Neohesperidose (2-O- α -L-rhamnopyranosyl-D-glucopyranose) is another characteristic disaccharide forming glycons in glycoside combinations [Muley et al. 2009, Arora et al. 2013, Colombo et al. 2015].

APPLICATION IN MEDICINE

In modern phytotherapy, as in folk medicine, *C. officinalis* flower extracts are widely used mainly in the treatment of dermatological diseases (Tab. 3) [Basch et al. 2006, Muley et al. 2009, Arora et al. 2013]. Many scientific studies on this species focused on anti-inflammatory and accelerated wound healing properties [Ukiya et al. 2006, Parente et al. 2012, Farahpour 2014, Buzzi et al. 2016, Nicolaus et al. 2017, Alexandre et al. 2018, Paul et al. 2018]. Anti-inflammatory activity is conditioned by the presence of terpenoid compounds (Fig. 2 and 3, Tab. 1 and 3), the higher the content of these compounds, the stronger the effect of the extract [Ukiya et al. 2006]. It has been proven that the use of an ointment with *C. officinalis* inflorescence extract reduces the incidence of dermatitis in people with breast cancer undergoing radiotherapy [Pommier et al. 2004]. In addition, ointments applied to skin wounds accelerate their healing by increasing epidermal epithelization [Paul et al. 2018]. New research indicates that *Calendula officinalis*-loaded poly ϵ -caprolactone/gum arabic nanocomposite scaffolds, when applied on wounds, increase cell adhesion and proliferation as well as have an antibacterial effect. This composition is well suited for skin regeneration [Pedram Rad et al. 2019]. Extracts of *C. officinalis* inflorescences can also be used for hard-to-heal wounds, such as venous ulcers, burns and other skin changes that are difficult to heal [Buzzi et al. 2016, Duran et al.

2005]. According to the latest research, preparations containing marigold flower extracts can be used in non-invasive and delicate therapies, difficult-to-treat plantar papules, painful hyperkeratotic changes and inflammation of the *hallux valgus* [Duran et al. 2005, Singh et al. 2011] (Tab. 3).

Extracts from *C. officinalis* inflorescences have scientifically proven antiviral, antibacterial, antifungal and antiprotozoal activity. Based on scientific research, it has been proven that *C. officinalis* extracts inhibit the activity of herpes and influenza virus, they also reduce HIV replication [Ukiya et al. 2006, Muley et al. 2009, Arora et al. 2013, Farahpour 2014, Salehi et al. 2018]. Extracts have an antibacterial effect on numerous strains of Gram (+) bacteria (incl. *Bacillus subtilis*, *Peptostreptococcus micros*, *Staphylococcus aureus*) and Gram (–) bacteria (incl. *Escherichia coli*, *Furobacterium nucleatum*, *Porphyromonas gingivalis*, *Pseudomonas aeruginosa*, *Veilonella parvula*, *Vibrio cholerae*) [Singh et al. 2011, Khalid and Silva 2012, Shankar et al. 2017, Lovecka et al. 2018, Muley et al. 2009]. In addition, it has been proven that *C. officinalis* essential oil has a stronger inhibitory effect on pathogenic fungal strains than nystatin [Khalid and Silva 2012] and inhibits the growth of the protozoan *Trichomonas vaginalis* [Samochowiec et al. 1979] (Tab. 3).

Scientific studies have demonstrated that extracts of *C. officinalis* inflorescences have antioxidant, spasmolytic, antidiabetic and hypolipemic effects [Cordova et al. 2002, Muley et al. 2009, Singh et al. 2011, Xuan et al. 2016, Lima et al. 2017] (Tab. 3). In addition, the latest report showed their pancreas-regenerating, hepatoregenerative, cardioprotective and neuroregenerative activity [Muley et al. 2009, Singh et al. 2011, Toropova et al. 2017]. Furthermore, triterpenoid glycosides found in *C. officinalis* inhibited the growth of tumor cell lines: colon cancer, breast cancer, leukemia as well as melanoma in *in vitro* tests [Muley et al. 2009, Farahpour 2014, Ukiya et al. 2006]. In addition, the *C. officinalis* saccharide group was shown to act immunostimulatory [Muley et al. 2009, Arora et al. 2013] (Tab. 3).

A detailed description of the mechanisms of extracts' biological activity and/or individual components of *C. officinalis* is presented in Tab. 3.

COSMETIC APPLICATIONS

Calendula officinalis is a popular species in the cosmetics industry, especially due to the scientifically proven anti-inflammatory, antioxidant and skin damage granulation accelerating properties [Anuradha et al. 2015]. *Calendula* is present mainly in the composition of cosmetics that have soothing, softening and regenerating effects.

Recently, an increasing popularity of preparations based on extracts from *C. officinalis* has been observed. Therefore, research focused on the cosmetic application of *C. officinalis* flower extracts is of particular interest. *In vitro* studies on skin cells with induced oxidative stress have proven that ethanol extracts from *C. officinalis* flowers have a strong antioxidant effect, and protect cells from damaging effects of UV radiation [Xuan et al. 2016]. Other studies have shown that cream with *C. officinalis* flower extract stimulates skin cell regeneration, improves elasticity, and also induces increased skin hydration, as a result of lower TEWL (transepidermal water loss) [Buzzi et al. 2016]. It has also been proven that cream with *C. officinalis* inflorescences reduces sebum secretion and has a brightening effect through the reduction of melanin content in the skin [Jadoon et al. 2015, Tundis et al. 2015]. Scientific studies have also demonstrated that the anti-aging effect of *C. officinalis* inflorescence extracts is related to the control of metalloproteinase (MMP-2 and MMP-9) secretion [Tundis et al. 2015].

Calendula officinalis oil is also applied in cosmetology. It has been proven that it has a stronger inhib-

itory effect on pathogenic fungal strains than nystatin [Khalid and Silva 2012] (Tab. 3). When used in emulsions, it accelerates wound healing and protects against UV radiation [Okuma et al. 2015, Lohani et al. 2018,]. In addition, the oil has a stronger antioxidant activity than geranium oil [Lohani et al. 2018].

According to Cosmetic Ingredient Database [CosIng] – an on-line database of cosmetic ingredients introduced by the European Commission – *C. officinalis*, is a species that can be used in ten different forms (Tab. 4). Interestingly, recently, the Bulgarian company Innova BM patented and introduced to the market two innovative cosmetic preparations based on *C. officinalis* cell cultures – with moisturizing, anti-aging and regenerating properties [Georgiev et al. 2018].

FOOD APPLICATION

In the past, marigold leaves were used in cuisine as a vegetable. Also today, fresh marigold flowers are added to salads. Dried flowers, as a substitute for saffron, are a spice for soups and cakes; moreover, they are used for coloring of, among others, rice, fat (margarine) and yellow cheeses. The safety of marigold flower use in food is confirmed by the European Food Safety Authority [EFSA] documentation.

SAFETY OF USE

Caution should be exercised with allergy sufferers when using or consuming preparations containing

Table 4. *C. officinalis* in the cosmetic products acc. to CosIng database

| Name acc. to CosIng | Cosmetic activity |
|--|---|
| <i>Calendula officinalis</i> extract | skin conditioning |
| <i>Calendula officinalis</i> callus extract | skin conditioning, skin protective, emollient |
| <i>Calendula officinalis</i> flower | skin conditioning |
| <i>Calendula officinalis</i> flower extract | skin conditioning, masking, perfuming |
| <i>Calendula officinalis</i> flower oil | skin conditioning, masking, perfuming |
| <i>Calendula officinalis</i> flower water | masking, flavouring, perfuming |
| <i>Calendula officinalis</i> flower/leaf/stem juice | skin conditioning |
| <i>Calendula officinalis</i> meristem cell extract | antioxidant |
| <i>Calendula officinalis</i> seed oil | skin conditioning |
| Hydrolyzed <i>Calendula officinalis</i> flower extract | skin protective |

marigold extracts or oil. Special care must be taken by people who are allergic to species from the family *Asteraceae* [Corazza et al. 2014, Denisow-Pietrzyk and Pietrzyk 2019]. The most common reaction is skin allergies (contact sensitization), as reported by the American Food and Drug Administration [FDA, Reider et al. 2001] and European Medicines Agency [EMA].

CONCLUSIONS

Marigold flower is currently a widely available raw material, valuable in terms of biological, medicinal, cosmetic and food properties. Research studies confirmed strong anti-inflammatory and antioxidant properties of this raw material; in addition, they demonstrated other very important effects of its biological activity, such as hepatoregenerative, cardioprotective, neuroprotective and anticancer properties.

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